

administration of ganciclovir, foscarnet, and most recently, cidofovir, for the treatment of CMV retinitis. Both in-office administration and surgical implantation of long-acting, slow-release reservoirs are used, with the intraocular implants having only recently received FDA approval. These techniques are extremely effective, and their use seems most indicated for patients with active retinitis close to the optic disc or macula or for whom parenteral therapy is contraindicated. Intraocular delivery, however, whether by direct administration or implant, carries the added risks of intraocular infection, hemorrhage, and retinal detachment. Moreover, local therapy does not protect the other eye or treat concurrent CMV disease in distant organs. Many ophthalmologists will, therefore, supplement local therapy with oral ganciclovir as tolerated.

There is currently no single best drug for the treatment of CMV retinitis in all patients. The selection of an appropriate antiviral agent needs to be tailored to each patient and based on a careful consideration of the location and extent of ocular and systemic disease, an understanding of previous and possible drug-related side effects, and a knowledge of the viral response to past treatments. Although CMV retinitis remains a major cause of ocular morbidity in patients infected by HIV, new and investigational therapies provide hope for effective long-term treatments in the near future.

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## Photorefractive Keratectomy

IN LATE 1995, the US Food and Drug Administration (FDA) for the first time approved a device to be used for the surgical correction of refractive error. This device, the excimer laser, is used to alter the corneal curvature by removing tissue from the corneal surface with minimal damage to the underlying cornea. A new geometry is thereby conferred to the surface of the cornea to reduce or eliminate one of the following forms of refractive error: myopia (nearsightedness), hyperopia (farsightedness), or astigmatism (in which the cornea has nonuniform curvature).

The 193-nm excimer laser has a special form of photon-

tissue interaction that makes it uniquely applicable to this type of surgical treatment. Tissue is removed through a process known as photoablative decomposition, in which molecular bonds are disrupted and a gaseous cloud of material is ejected from the corneal surface with each pulse. There is minimal damage (thermal or otherwise) to the underlying corneal tissue, so that in most cases the cornea retains a high degree of clarity as it heals from the operation.

Two laser manufacturers have conducted large multicenter clinical trials and obtained approval from the FDA to market their devices. The approval at this time is limited to the indication of myopia. In the United States, estimates are that 90% of persons with myopia have 5 diopters or less of myopia. Because the approval from the FDA extends to those with as much as 6 or 7 diopters, most myopic persons are possible candidates for this procedure.

The efficacy of photorefractive keratectomy has been clearly established. About 94% to 95% of patients will achieve 20/40 or better vision, without glasses or contact lenses, as a result of the procedure. This is the level of vision required to pass a driver's license vision test without correction. On the other hand, this level of vision often is not adequate to allow all patients to perform all activities without correction. The percentage of eyes that achieve 20/20 vision is related to the severity of the nearsightedness being treated, but is substantially less than the likelihood of achieving 20/40 vision. Overall in the studies, about 50% to 55% of eyes treated with this procedure achieve 20/20 vision.

Patients considering excimer laser photorefractive keratectomy need to understand that there is a small but well-quantified risk to vision with this procedure. About 1% of patients have a loss of best-corrected visual acuity as a result of the procedure. By definition, this means that after the operation, patients cannot be corrected with glasses back to the level of vision that they had before the operation. Thus, a person who sees 20/20 with glasses before the operation may no longer see 20/20 after it, with or without glasses. Therefore, when weighing the decision to have the operation, patients need to consider the possible effects of this loss of vision and carefully weigh the risks of the procedure against the perceived benefits. Perceived benefits often cited by patients who are considering or who have had refractive surgery include the following: decreased dependence on corrective lenses, avoidance of discomfort associated with contact lens wear, and the ability to participate in sports or occupations in which the use of corrective lens wear is problematic.

The procedure is done on an outpatient basis using topical anesthesia. The patient is instructed to fixate on a target while the surgeon centers the laser. The corneal surface epithelium is removed, and the corneal stroma is then reshaped by the laser according to a computer-determined algorithm that is based on the preoperative measurements of the refractive error. After the operation, the eye is treated with topical antibiotic and anti-inflammatory medications and often a thin, soft contact lens until the corneal surface has healed. Although the procedure itself is painless, patients may have mild to moderate, or

occasionally more than moderate, "pain" during the first day or two after the procedure.

Not everyone is an appropriate candidate for excimer laser photorefractive keratectomy. Coexisting severe ocular disease, such as glaucoma or dry eye, may disqualify a patient from consideration. In addition, it is important that patients have appropriate expectations regarding the outcome of the procedure. A patient who wishes to reduce dependence on corrective lenses for most activities of daily living may be an appropriate candidate, but a person who demands "perfect" uncorrected vision after surgical treatment and a total elimination of spectacles or contact lenses for all tasks should be counseled not to have the procedure at this time.

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## New Agents for the Treatment of Glaucoma

GLAUCOMA is a disease state where the intraocular pressure is too high for the health of the optic nerve. This causes a progressive but treatable optic neuropathy affecting 5 to 10 million North Americans. At a clinical detection rate of 50%, upwards of 116,000 people in the United States are blind in both eyes as a result of this disease. Glaucoma is more common among elders in whom a large number of concurrent medical conditions may exist. Existing agents used in the treatment of glaucoma may have decreased usefulness in this patient population because of preexisting or developing cardiopulmonary problems, allergy, depression or other alterations in mentation, nephrolithiasis, or induced visual disturbances. Clinicians caring for patients with glaucoma have welcomed the introduction of two new agents for the treatment of the disease.

Latanoprost 0.005% (Xalatan) is a new phenyl-substituted prostaglandin (PGF $\alpha$ ) analogue. It is the first drug in a new class of ocular hypotensive agents. Extremely potent, it is a lipophilic prodrug that is activated by enzymatic hydrolysis of an ester linkage. It has an unusual mechanism of action: it increases the uveal scleral (non-trabecular) outflow. Agents affecting trabecular outflow or aqueous production have a pressure-lowering limita-

tion set by the episcleral venous pressure. Latanoprost, therefore, has a theoretical advantage because intraocular pressures can be lowered below the episcleral venous pressure. Before US Food and Drug Administration approval, this pharmaceutical agent was studied in more than 800 patients at three separate centers in the United States, Great Britain, and Scandinavia. In Great Britain and Scandinavia, it was found to be equally efficacious to timolol maleate 0.5% (Timoptic). In the United States, it was found to be more efficacious ( $P < .001$ ) than timolol maleate 0.5%. In these studies, foreign body sensation, stinging, punctate epithelial keratopathy, and pain occurred with both agents to varying amounts. Conjunctival hyperemia, although mild and primarily cosmetic, was more common in patients treated with latanoprost ( $P < .001$ ). Although the cardiopulmonary safety profile of this agent is excellent, it does produce an interesting ocular side effect. The use of this agent can result in a progressive darkening of the iris (10%). This effect has been extensively investigated and has found to be due to the increased production of melanin by melanocytes and is not related to an increased number of melanocytes.

Brimonidine tartrate 0.2% is a potent and highly selective  $\alpha_2$ -adrenergic agonist that decreases the intraocular pressure by decreasing aqueous production and increasing uveal scleral outflow. Brimonidine is the second agent available for use in the treatment of glaucoma in the  $\alpha$ -adrenergic agonist class. It differs from apraclonidine hydrochloride (Iopidine) by the addition of a quinoxaline ring system to the parent molecule and use of bromine rather than chlorine substitution. Brimonidine has been shown to be 30 times more selective than apraclonidine for the  $\alpha_2$ - versus  $\alpha_1$ -adrenergic receptors. In clinical trials at twice-a-day dosing, brimonidine tartrate 0.2% has been more efficacious than betaxolol hydrochloride (Betoptic-s 0.25%, twice a day) and comparable in efficacy to timolol maleate 0.5% (Timoptic 0.5%, twice a day). Tachyphylaxis with the use of brimonidine has not been a notable problem, but ocular allergy ( $P < .001$ ), dry mouth ( $P < .001$ ), and conjunctival follicles ( $P = .001$ ) were more common in patients treated with brimonidine, whereas burning and stinging were more common in patients treated with timolol maleate ( $P < .001$ ). Drowsiness occasionally occurs with use. These two agents are effective and welcome additions to the glaucoma armamentarium.

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